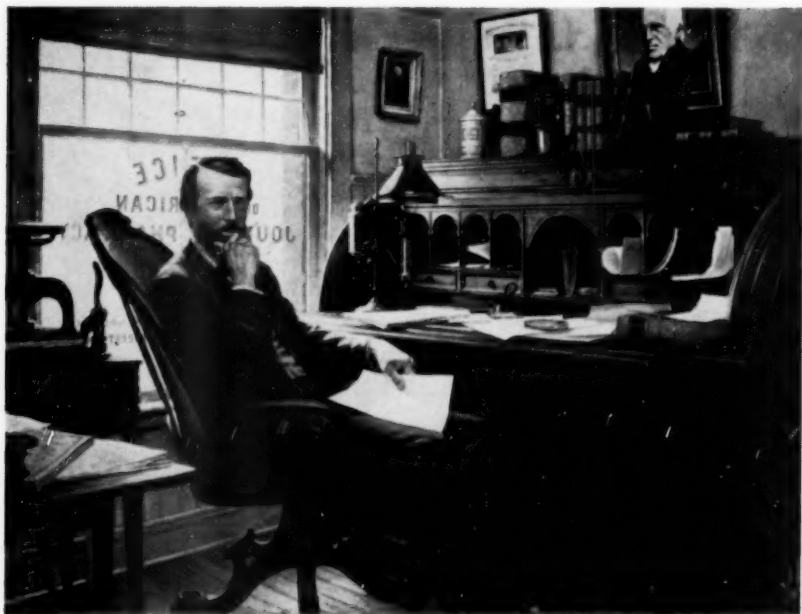


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AND THE SCIENCES SUPPORTING PUBLIC HEALTH



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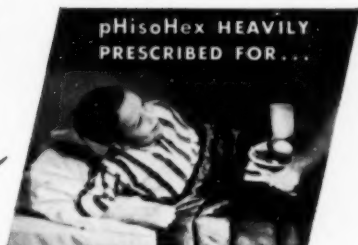
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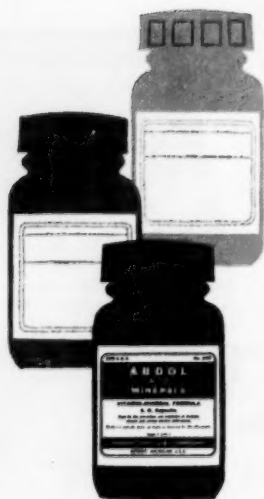


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AND THE SCIENCES SUPPORTING PUBLIC HEALTH

Since 1825

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## O U R C O V E R

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THE Journal this month has on its cover a photograph of the painting of William Procter, Jr. recently completed by Richard Thom, the artist who has painted the Parke-Davis series. While we admit some prejudice, it is our opinion that this painting of Procter is possibly the best one yet achieved in this remarkable and outstandingly good sequence. The impact of the original painting on the viewer is tremendous. One can almost feel the full depth and character of that great man who so deservedly is known as the father of American Pharmacy.

Rather than attempt to write an editorial suitable to grace this issue of the Journal we have chosen to republish a Valedictory Address given by the great Procter to his graduates in the year 1858.

At that time Procter was Professor of Pharmacy and Editor of this Journal. He was exactly as he has been painted by Thom, a vibrant and powerful personality and one dedicated to his profession. His message as given then might well be given today, insofar as its philosophy and integrity of purpose are concerned. While our drugs have changed, the truly meaningful things of life and the profession have not. We commend it to your reading.

THE EDITOR

## VALEDICTORY ADDRESS TO THE GRADUATES OF THE PHILADELPHIA COLLEGE OF PHARMACY,

Delivered March 11th, 1858, at the Musical Fund Hall \*

By William Procter, Jr.

**G**ENTLEMEN:—A time-honored custom requires that the ceremonial which has just been witnessed, should be followed by a word of gratulation and advice; and the duty of conveying it to you, on this interesting occasion, has devolved upon me.

The old relationship of teacher and pupil having ceased, permit me to welcome you into the ranks of the pharmaceutical profession, as qualified to take part in its duties and its requirements, and determined to win the honors and emoluments to which a faithful fulfilment of them will justly entitle you.

The steps by which you have gained your present position have been many and tedious; marked with numerous trials calculated to discourage your progress. These accidents of fortune have not proved injurious;—the blasts that assail the hill-side oak but develop its internal power of resistance, intertwine more closely its fibres, and consolidate its tissues;—so the difficulties of your novitiate,—your apprenticeship,—have tended to bring out your latent qualities; stimulate your ingenuity; teach you the power of patience, the force of endurance, and the all-conquering influence of perseverance, when directed to the attainment of an education in Pharmacy.

The profession you have adopted is among the most respectable that engage the attention of men; its results are directly beneficial to the community, when its practice is in the hands of qualified individuals; and without its aid the physician is greatly circumscribed in his ability to restore the sick to health and enjoyment. The function of the apothecary is one of great responsibility, in so far as he is the custodian of the powerful agents by which cure is effected. Ignorance or carelessness on his part may wholly defeat the wisest

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\* *Extract from the Minutes of the Board of Trustees, March 9, 1858.*

*"Resolved, That Prof. Procter be desired to furnish a copy of his Valedictory Address to the Graduating Class, at the coming Commencement, for publication in the American Journal of Pharmacy."*

ALFRED B. TAYLOR, *Secretary.*

diagnosis, and most appropriate prescription; may baffle the physician in his endeavors to cope with disease; and even consign the sufferer to an untimely grave. In this view, then, the claims of Pharmacy to rank as an honorable calling, involving regular studies and skilful practice, will not be disputed; nor will the pharmacist, when worthily engaged in its legitimate offices, fail to receive the respect and support of the community in which he may be located.

The history of Pharmacy, as it *was* and as it *is*, is a curious and interesting study, even to the non-professional inquirer. In the earlier ages it was included in the occupation of the physician; but a few years have elapsed since this union was severed in the cities of the United States, and at this time many instances occur, where the duties of physician and apothecary are united in the same individual. They are, nevertheless, distinct avocations, tending to the same end; between them a mutual check reaction occurs, healthful to each class.

It is not my purpose, however, to occupy our time this evening with the records of the past, full of teaching as they are to those who consult them earnestly; yet it seems entirely appropriate on an occasion like the present, when a numerous representation from the community in which we live have honored us by their presence, to present a view of the true character of the duties which Pharmacy owes to Medicine and to the community, with the obligations due by these in return.

In the long course of ages, medical observers, aided by accident, have detected a curative power in numerous substances existing in nature. So universal is the necessity for medical aid, that men in all countries agree in promoting the discovery of every thing capable of increasing its power and certainty; and in enlightened countries of the present day, the care and preparation of these agents has been committed to a distinct class, known as apothecaries, pharmacists, or chemists and druggists.

It has been elsewhere said, that the three primary duties of the pharmacist are "to procure and keep good drugs;" "to prepare from these efficient and uniform medicines;" and "to dispense these medicines to the sick, in a perfect condition."

To perform the first of these judiciously, the apothecary must know the nature and qualities of drugs, their tendency to deteriorate by age and exposure, the means of preserving them in the best man-



ner, and lastly, he must conscientiously practice what he knows, the most difficult and often the least appreciated portion of his duty.

The study of drugs involves much scientific knowledge, leads the student into botany, mineralogy and other branches of natural history, and chemistry is largely concerned in judging of their quality. He will often observe an adaptation of means to ends in the production of medicinal substances, not less wonderful than in other results of creative power. The bark of the wild cherry tree is highly prized by the physician, for a remarkable association of tonic and sedative powers, extremely useful in pectoral and cardiac diseases. The principle upon which this sedative influence depends is prussic acid; the same volatile, evanescent substance, which, when made by the chemist, is so powerful a poison; and which, did it exist ready formed in the bark when gathered, would soon evaporate and leave it nearly worthless on drying. But so useful a drug has not been left liable to certain deterioration;—stored safely in the tissues of the bark are two distinct substances, neither of which is the medicinal acid, but when they come together in the presence of water, a chemical reaction occurs, and from the twain comes the valuable sedative full of healing power. It has been shown by one of your predecessors, that the value of this bark varies with the season of its collection, having double the strength in October that it has in May; and the well-informed apothecary, knowing this, avoids gathering the drug in the spring or summer.

The trees producing the Peruvian bark are found on the eastern slopes of the South American Andes, stretching from near the Caribbean Sea to the Bolivian Republic, growing at an elevation varying from 5000 to 9000 feet above the level of the sea. Many species of this tree exist, yielding barks of various quality and medical value; some containing much quinine, others little, if any. The collectors of the bark are liable through ignorance, or tempted by gain, to substitute one for the other. How shall the apothecary, thousands of miles away from the lofty Cordilleras, where the bark is gathered, be able to avoid the results of this ignorance, or fraud, and shield the sick from the effects of the inert substitution? You, Gentlemen, can reply to this question, that you have been taught by the nice means of discrimination, by which the genuine are distinguished from the spurious, or the bark of one species from that of another, by the color, the taste, the structure, the mosses that grow

on their surfaces, but, beyond all other means, by that magical power of the chemist, which compels each bark to give up its secret strength, in kind and quantity, to his scrutinizing examination.

Among the natural causes which determine the value of medicinal substances, climate and soil exert a most remarkable influence. Fox-glove, so valuable as an arterial sedative in Europe, is shorn of half its power, when grown in the United States; Opium, when obtained in Turkey, differs materially, both in power and composition, from that produced in the valley of the Nile; and these, again, from the varieties raised in central India for the consumption of China. In the recesses of Chinese Tartary, carefully excluded from observation by the celestial policy, grow those valuable species of Rhubarb, yielding the best varieties of the drug, which, after centuries of medical experience, continue to hold a prominent position among the indispensables of the *Materia Medica*. Various efforts have been made to introduce these plants into Europe, and with apparent success; but though they grow with luxuriance, the principles upon which their medicinal value depend are but imperfectly developed; and as medicines, they are unfit to replace their oriental progenitors. Notwithstanding this fact has been proven and carefully recorded, thousands of pounds of European rhubarb are annually thrown into commerce, and consumed, not on its own merits, but as a cheap means of adulterating the more costly varieties of the East. Some of this European root rivals the genuine in the beauty of its internal structure and coloring; but its odor, and taste, and chemical composition, cease to correspond. From some local peculiarity of soil, oxalic acid combined with lime, is largely an ingredient in Tartarian rhubarb, whilst this salt is very slightly found in the product of England and France; thus affording to the pharmaceutical chemist an unfailing criterion for detecting this fraudulent substitution, when other than ocular evidence is needed.

The natural causes of deterioration in drugs are, therefore, sufficiently obvious to require the watchful care of the apothecary to avoid their hurtful influence; but when to these are added the results of a wicked trade in adulterations, applicable to nearly every valuable item of the *Materia Medica*, the utmost prudence and acuteness is called for to avoid imposition. Cream of tartar, the pure acid salt of grape juice, is mingled with alum and vitriol; chalk, gypsum and barytes have been admixed with calomel; and the oil of lemons,

so delightful for its fragrance, is reduced with the spirit of turpentine. In the means of recognising genuine, and detecting adulterated and spurious drugs, there is, Gentlemen, an ample field for the exercise of your experimental talents, and I trust you will enter it with enthusiasm, and partake of the pleasure, as well as reap the honors, which accrue to the successful prosecutor of this important and interesting branch of pharmaceutical investigation.

The conversion of drugs into efficient and uniform medicines, fitted for administration to the sick, requires the skill derived from practical experience; hence the importance placed by our College on a regular four years' apprenticeship, to acquire the details of the business. The purest and best drugs may become inert and valueless by unskilful preparation; compounds of safe and efficient powers may become poisonous, and changed in character, by careless manipulation and ignorance. The physician may have his faith in remedies destroyed by the use of ill-prepared samples, wholly unconscious of the short-coming of the apothecary upon whom he relied. It is the pride of the able pharmacist to render his preparations efficient in power, and beautiful in appearance; the contrast of the adept and the pretender is so perceptible in this department of the business, that the public eye will draw the distinction, in the transparency of syrups, the fineness of powders, and the creamy smoothness of ointments, when unable to judge of their medicinal power. If it is so important to attend to these visible, though not always essential evidences of care, how much more necessary is it to scrupulously effect the accurate combination of ingredients in the officinal preparations? By neglecting this care, precipitated sulphur may become contaminated with twice its weight of plaster of Paris; calomel, by careless washing, may contain corrosive sublimate; glycerin may be affected by sensible portions of lead, and vegetable extracts by copper, from the use of ill-conditioned apparatus.

Gentlemen, the lessons you have learned in the laboratory and at the lecture room have taught you to avoid these errors, and they should not be forgotten, but by practice and study should be rendered more and more effective.

If the selection of drugs and the preparation of medicines involves so many requisites, the dispensing of these to the sick, by the prescription of the physician, calls for a higher qualification and a wider experience. Whatever knowledge he may have gained, to

whatever extent his ingenuity may have been stimulated, however much his patience and care may have been cultivated, the conscientious apothecary finds ample scope for their exercise and employment in this division of his daily engagements. If he would avoid error, the dispenser must do nothing without the consent of his *will*; he must be conscious of every act that he performs, and shun *mental preoccupation* as he would the fabled influence of the poison upas, as it is the *true* source of most of the fatal mistakes, strictly due to the apothecary, which the annals of Pharmacy occasionally record. In reading a prescription the dispenser has not only to understand what is written, but he should feel satisfied that what it calls for is intended by the physician. Although, legally, the recipe of a physician is a sufficient guarantee to dispense any poison or composition, yet the pharmacist, when duly impressed with the responsibility of his office, feels morally bound to extend a rational judgment in reference to the prescription he dispenses, as well in justice to the prescriber, as to the patient and himself.

The exercise of this watchful supervision requires the greatest delicacy and discretion, when it leads the apothecary to believe he has detected an error. It is a matter solely between the physician and himself. He may find, on inquiry, that some peculiar condition of the patient required the unusual dose, and that his own judgment was wrong. Hence nothing short of a feeling of duty, based on the utmost certainty, should cause him to doubt the literal meaning of a physician's prescription, except in cases of omission.

Fortunately the need of this interposition is rarely required, and would be yet more infrequent, but for the thoughtlessness of those who are near the physician when engaged in writing his prescription. During this important act, when his faculties require to be concentrated on the requirements of the case, when a long list of medicines have to be selected from and associated, when the numerical proportions of these have to be calculated and symbolized, and the dose duly ascertained and indicated, he is frequently interrupted by the attendants with ill-timed and irrelevant questions, or by relatives with expressions of excited feeling, tending to distract his attention.

The subject of the custody and sale of poisons is of serious interest to the pharmacist. By the fiat of the Creator a large number of plants and minerals are noxious to animal life. Of these, many rank as eminently valuable medicines; others are used chiefly in the

arts and sciences, and are kept by the apothecary and druggist. Not only has he to dispense these poisons by prescription, but many are habitually sold by the druggist, and bought by the people, without other license than that which creates the demand with the consumer, or which a sense of moral responsibility calls forth in the dispenser. Except in a few isolated localities, no legal regulations exist to restrain this traffic, and each dealer, be he druggist or apothecary, grocer or storekeeper, is left to pursue such policy in regard to it as he may deem expedient.

Until quite recently the same unrestrained trade existed in England, but Parliament, aroused by the frequent occurrence of accidental and murder poisoning, appointed a committee to frame a bill for the regulation of the sale of all poisonous agents. This committee has been in session for many months past, and have not yet perfected the draught of a law, owing to the numerous difficulties that arise when the attempt is made to render the law practically efficient, and at the same time not burdensome to the legitimate dispensing of medicines by pharmaceutical chemists.

So impressed was the American Pharmaceutical Association, at its late meeting in this city, with the practical difficulties that present in framing a statute to meet the evils of poisoning, that they preferred to confine their action to a circular of advice to apothecaries and druggists, rather than recommend legislative interference, believing that a large number in all parts of the United States have adopted regulations for this traffic in their own undirected sense of its propriety.

Gentlemen, you need hardly be reminded of the precepts you have received from us in relation to this subject; nor will I doubt but that they will ever be remembered in your professional intercourse with the public. Toxicology, or the science of poisons, in its medico-legal aspect, is part of the acquirements of the thorough pharmaceutical chemist. He should be able to make investigations when duty calls him; but, let me advise you, leave such engagements for the *professional chemist*; do not seek these occasions of public notoriety, as the time consumed in the process, and the annoyance of judicial cross-questioning by opposing attorneys, to baffle and confuse your evidence, will more than outweigh the satisfaction that may arise from vindicating the power of science when exhibited in the service of justice.

Let us now take a view of the relative position of the dispenser and the community or neighborhood in which he is located. When an apothecary shop is opened, the proprietor tacitly, if not verbally, announces that he has prepared himself with the knowledge, skill and material required to perform the responsible duties that appertain to his vocation: each family around him have a direct interest in the truthfulness of this annunciation, as, sooner or later, all may be brought to the necessity of testing it practically. The nature of this knowledge and material is but obscurely understood by them; the pure and the impure, the inert and the poisonous, the true and the genuine, may be taken by each family in the confidence they repose in the ability and honesty of their dispenser. Gentlemen, mark this beautiful relationship! reflect on the almost child-like reliance which sends the family messenger to you for aid for its afflicted member! How priceless is the value of a pharmaceutical reputation, when exalted by knowledge and skill, and adorned with conscientiousness and integrity; and with what jealous care it should be tended that its brightness be not tarnished.

Like the physician, though in a different manner, the apothecary becomes the recipient of much that pertains to the unwritten history of his neighbors. In moments of distress, when the delicate equilibrium of organic forces which result in health, are harshly assaulted by the emotions, chapters are opened which give insight into unseen and untold episodes of humanity. To his ear, poverty-engendered illness brings many a tale of mental and physical suffering, which else had remained untold and quietly borne until better times smiled on their subjects. He often beholds the secret motives which influence public actions; he can understand the brilliancy of many a speaker and actor on the surface of public life, and trace it to opium or chloroform. He can sometimes detect the primal efforts of the suicide and poisoner; to him comes the incipient, and yet shame-faced, inebriate, to get relief from the effects of his early aberrations, whilst he still regards a reputation for sobriety; and to him often applies the victim of unhallowed love, for aid in her last extremity, when despair, gathering its darkening folds around her, pictures the future an unfathomable abyss of blackness and woe.

Nor is it always in the darker phases of mental outpouring that the dispenser of medicines becomes the recipient of human confidence. Family joys as well as sorrows find utterance. He is often made a



witness of the bright aspirations which arise on the occasion of the safe accession to the family circle of a new candidate for parental care and responsibility. When the wanderer has returned to his home, stricken with disease, the pleasure that wells up among its inmates is shared by the apothecary as he listens to the gladdened accents of a parent or brother, whilst preparing something for the relief of the sufferer. These confidences and opportunities are not restricted to a single class; all shades of society become objects of interest to the intelligent dispenser; and he should let discretion govern his tongue, and wisdom his actions, in relation to all that transpires of private history in his intercourse with those who frequent his establishment.

Gentlemen, you who are dispensers of medicine, need I caution you further in regard to your professional pathway? The precepts you have received and the practical training you have experienced have instilled into you the length and the breadth, the height and the depth of its varied requirements. Let me entreat you to keep them green and fresh in your memories; let a sense of professional honor keep you in the line which has been marked out for your pursuit; let no temptation allure you into a compromise with principle; determine to execute your known duties, in the right spirit, and the reward will be the confidence, respect and patronage of your friends and neighbors.

Some of you propose to pursue the vocation of a druggist or wholesale dealer in drugs for supplying the dispenser. Are *you* fully imbued with a knowledge of its peculiar responsibilities? Are *you* prepared to resist the temptation to sell worthless drugs, held out by the demands of the ignorant and unprincipled, to whom cheapness is the rule? have you determined to exercise the knowledge and skill, just now so honorably accorded to you, in upholding the quality of imported drugs, and in protecting the well-disposed, though ignorant, who may come to you in good faith to purchase their stock? Too many there are who buy and sell drugs, wholesale, without a thought of their object as means of cure, as agents, upon the quality of which the lives of their fellow men may depend. A real incident, which occurred to a friend of mine in New York, is so much to the point in illustration of this fact, that it may be safely adduced. This friend, who I shall call Colton, and who at that time was an eminent pharmacist on Broadway, having occasion to replenish his stock of cantharides, or blistering flies, called on the druggist, with whom he

usually dealt, to procure them; but he having none, application was made to another druggist, who shall be called Haswell. Entering the extensive establishment of the latter, the following dialogue ensued:

*Colton.*—"I am informed that you have powdered cantharides of good quality, and I am desirous of getting some that is reliable."

*Haswell.*—"Oh certainly! you will find none better; we had the powder made expressly for our sales, from selected flies."

*Colton.*—"I am particular in providing this drug, as you know how much depends on its efficient and prompt action."

*Haswell.*—"You may rely upon our article as in good condition."

Here the conversation closed, Colton gave his order, and left the store. Some weeks after, while he was engaged at his counter, Haswell walked in, evidently under some nervous excitement, when the following occurred:

*Colton.*—"Good morning, Mr. Haswell, can I serve you today?"

*Haswell.*—"A member of my family has been taken suddenly ill; her physician, among other treatment, has prescribed a blister, and I have come out of my way, believing from your well-earned reputation that we may rely on your cerate, and much depends on the rapid action of the plaster."

*Colton.*—"I have always been careful in preparing this cerate from good flies, and fortunately, in this instance, I have your own testimony in addition, in their favor."

*Haswell*, who had till that moment forgotten the first transaction, quickly replied, "But, sir! are you sure those flies were active? have you tried them?"

*Colton.*—"You *said* they *were* when you sold them to me."

*Haswell.*—"But, my dear sir, this blister is for my *daughter*! Don't you understand me? for my *only daughter*! Can I rely upon it?"

*Colton.*—"FOR YOUR DAUGHTER! And so my cerate is for every other man's daughter who deals with me, and who may need it, and who is as dear to his affection as yours is to you. When I purchased those flies from you, it was your reiterated assurance of their re-



liability that chiefly induced me to take them, but now I perceive that your language had no real value, and that it was given in the spirit of a huckster. I trust, sir, that this incident will be of use in your future transactions; and for your present comfort I may assure you that your flies were found to be efficient, before they were dispensed."

Haswell acknowledged the justice of the reproof, and said, that never before had he been properly impressed with the responsibility attached to the wholesale drug business.

I am happy to be able to say that the drug market of the United States has been favorably affected by the gradual operation of the drug law passed by Congress in 1848, rendering all imported drugs and medicinal preparations subject to inspection, before passing the Custom House. At the port of New York, during the period of eight years that this law was administered by Dr. M. J. Bailly, the late efficient Examiner, the amount of spurious, adulterated and deteriorated drugs rejected and screened out of the market, was 900,000 lbs., which vast amount, but for this *law*, would have been scattered through the country.

The picture drawn by Haswell of the adulterations of food and medicines practised in England, as revealed to him by the microscope, is as interesting as it is deplorable, and forms the subject of a volume now accessible to the public. The power of Parliament is being directed to this subject, as it relates to Great Britain, and something may be done to diminish the evils of adulteration, which are now so extensively practised by the tradesmen and manufacturers of that industrious people. But it may be doubted whether we, as a nation, are much behind them, in regard to "home adulterations." The power of Congress is limited to the Custom House when it presents us foreign products in good condition. Once beyond the Examiner, they are open to the mercy of American ingenuity; the skill which evinces itself in the production of *genuine* French brandies, wines and perfumes, is not slow to enter the domain of medicines, and by the aid of modern alchemy, transmute the bitterness of willow bark, and the glossy fibre of the cotton boll, into veritable quinine of Pelletier and Caventou.

Legislation, to meet this evil in its home aspect, must originate and be carried into effect, by the authorities of each State; adulterating

medicines must be made a felony, punishable by statute, just as any other crime against the welfare of the public health. But amid the diversified interests striving for ascendancy at our legislative centres, such wholesome sanitary measures have little chance for a hearing; for, whilst even the reported approach of a pestilent epidemic will send forth stringent mandates, crippling commerce in their unsparing application of the laws of Quarantine, the perennial, ever present evils that we have pictured, flourish and extend, unheeded by the fathers of the State.

*My friends! we are about to part.* Before giving the sign let me tell you a *truth*—a truth which twenty-seven years of professional experience have but tended to confirm. *The only permanent cure for these evils is the union of knowledge, skill and integrity in the dispenser of medicines.*

As teachers, we have endeavored to give you the first. The second you have gained in the several establishments of your special preceptors. The *last* rests with yourselves. *It* is the crowning qualification, which, as worn or discarded, shall render you a blessing or a curse to the communities in which your future lots may be cast. Let me earnestly invite you, then, to wear it in its purity and unsullied brightness, as it applies to your professional duties in all their details. Rest not satisfied with that phase of integrity which relates to the payment of debts, and the *visible* rendering of what is due to your neighbors and customers. This much can be legally and socially claimed of you, and the merest regard for reputation will lead to their liquidation. But let your integrity be *felt* by the invalid in the seclusion of his chamber, through the purity and perfection of your medicines, in the care exercised in dispensing them, and in your intelligent attention to the requirements of the physician, as expressed in his written prescriptions. Let it be *manifested* by your resistance to those strong temptations to gain, which a mercenary system of empiricism holds out to the apothecary and druggist, which, too often, render them willing agents in the deception of the public; and finally in a uniform and indiscriminating attention to the medical requirements of your several neighborhoods. Integrity thus practised brings a reward as certain as it is priceless, a satisfaction that no money can buy, second only to that higher happiness which crowns the fast held integrity of the good man, who has unswervingly performed all his moral and religious duties. *Farewell.*

## SINCE 1825

By John E. Kramer \*

FOR the most part, advertising brochures are well done, but, as percentage response tables prove, most of them end up in the so-called "circular file." There was one, however, conceived recently by a book publisher, and sent to the writer, that not only stayed out of the waste basket, but sold its product. And chiefly because the sender was clever.

Typed at the top of this printed folder describing a new directory of business founding dates was this message: "Dear Mr. Kramer: It might interest you to know that your publication is one of 22 businesses listed in the Directory as having begun in 1825. It was a good year for publishing (to survive), four newspapers and Appleton-Century Crofts, besides your organization, having started then and are still in operation."

Naturally, our curiosity was aroused, and forthwith went the order for the book. And upon its receipt, we found the name of the *American Journal of Pharmacy* heading the list for 1825, with the well-known Appleton-Century Crofts Company next in line. Then follow the *Athens* [Ohio] *Messenger*, an evening newspaper; the *Boston Herald* and the *Boston Tribune*, morning and evening dailies respectively; and the *Kennebec Journal*, a morning paper published in Augusta, Maine.

A number of banks and insurance companies, and the Bigelow-Sanford Carpet Company were started also in 1825, and the directory reminds us that the Erie Canal was opened then, and the first locomotive to run on rails in America was operated experimentally in 1825 on a half-mile circular track in Hoboken, N. J.

But our interest lies chiefly in the *American Journal of Pharmacy*.

In the year of its founding, pharmacy in America was something considerably less than organized, and as a profession was in a none

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too enviable position. There were no particular laws governing its practice, and education in pharmacy was in its infancy, the Massachusetts College of Pharmacy having been founded only two years prior to the *American Journal of Pharmacy*, and only two years after the founding of the Philadelphia College of Pharmacy (1821) as the first institution of its type in the Western Hemisphere.

One of the objectives of the young Philadelphia College was the dissemination of pharmaceutical knowledge, culminating in the publication in December, 1825, of the *Journal of the Philadelphia College of Pharmacy*, through the coöperation of a publishing committee composed of Samuel Jackson, Henry Troth, Solomon Temple, Ellis H. Yarnell, and Daniel B. Smith, who, to all intents and purposes, acted as editor.

The lead article in this initial issue was Smith's "On the Preparation of Glauber's and Epsom Salt and Magnesia from Sea Water." What we would now call an editorial, but what was then termed "Introduction," was a treatise on the separation of the art of the apothecary from the practice of medicine, and from the selling of paint.

One year prior, in 1824, the College had prepared and printed a formulary for the preparation of eight patent medicines that it had adopted, and one year later, in 1826, a *Druggist's Manual*, or current price list of drugs and medicines, had been compiled and printed by the College. Other than that, however, pharmaceutical publications were practically unknown in this country.

After the first issue of the *Journal*, in 1825, three other numbers appeared (May, 1826, September, 1827, and November, 1827), then nothing until April, 1829, when regular publication was begun on a quarterly basis, under the editorship of Benjamin Ellis, who, unfortunately, lived only two more years, and then Robert E. Griffith was appointed editor. At the same time, the name of the publication was changed to its present title, the *American Journal of Pharmacy*.

As the *Journal* increased in stature and popularity, so did its frequency increase; as a quarterly until 1852, except in 1847 when five issues appeared, it was changed to a Bi-monthly in 1853, and was published six times a year until 1870. Then it was deemed necessary to provide an issue each month, and from that day to this it has appeared without fail, twelve times each year. The current Volume Number is 126.

The first paid advertising appeared in the issue for April, 1848, inserted by Lea and Blanchard, publishers of Philadelphia, extolling the virtues of their Dispensatory and Formulary. The first paid advertising for medicaments appeared in the October, 1850 issue, with George D. Phelps, importer of New York City, offering for sale such items as Brown's Cantharidine Blistering Tissue, Brown's Tissue Dressing, Cox's Celebrated Sparkling Gelatine, and others.

A remarkable feature of the *Journal's* history is the relatively low number, eleven, and the extremely high caliber, of the men who have guided its destinies through 128 years. Following Daniel B. Smith (1825-1828), Benjamin Ellis (1829-1831) and Robert E. Griffith (1831-1836) mentioned before, the following have served as editors: Joseph Carson, 1836-1850; William Procter, Jr., 1850-1871; John M. Maisch, 1871-1893; Henry Trimble, 1893-1898; Henry Kraemer, 1898-1917; George M. Beringer, 1917-1921; Ivor Griffith, 1921-1941; and Linwood F. Tice, from 1941 to date.

The *American Journal of Pharmacy*, today, still published and supported by the Philadelphia College of Pharmacy and Science, is a modern magazine, reflecting research in pharmacy and the allied fields, topical review, history, and editorial courage in its columns. Book reviews and medical and pharmaceutical abstracts are included in each monthly issue. The *Journal* has a large number of subscribers (it is one of the few subscription magazines left in the field of pharmacy), and it is sent also to every member of the College, and to a very long list of "exchanges" all over the world. Through this latter means, it is quite international in character.

And so, just as the publisher of the *Business Founding Date Directory* (which, incidentally was edited by Etna M. Kelley, and published by Morgan and Morgan, of Scarsdale, N. Y.) pointed out in his personal note on his advertising folder, we, too, point out each month on our masthead—"American Journal of Pharmacy, and the Sciences Supporting Public Health—Since 1825."

## THE RELEASE OF ALUMINUM ACETATE FROM OINTMENTS

By R. Frank, Pharm.\* and G. J. Stark, M. D.\*\*

**S**OLUTION of Aluminum Acetate (Burow's solution) is frequently prescribed as an ingredient in ointments for its soothing action on inflammations which is probably due to its astringent effects upon skin and mucous membranes.

For the same reason it also enjoys some popularity as a vasoconstrictor in nasal ointments, especially in pediatric practice.

As in the case of lead subacetate ointments which serve similar purposes the ointment bases used are either anhydrous lanolin and petrolatum (liquid petrolatum for nasal ointments) or an absorption base (consisting of higher monohydric alcohols, petrolatum and cholesterol esters) with added liquid petrolatum for nasal ointments. The solution of the astringent is incorporated into the bases to give a homogenous emulsion.

Although it should seem obvious that water-soluble, ionized compounds like aluminum acetate and lead subacetate, would diffuse better from a water-washable or water-soluble base than from a water/oil emulsion ointment, those latter bases are still in use in some official preparations, e.g., Ointment of Lead Subacetate B. P. C., Compound Ointment of Cinchocaine B. P. C. and Ungt. Plumbi Subacetici Ph. Helv.

The conclusions of various authors (1, 2, 3) that water-soluble antiseptics diffuse best from ointment bases of oil/water emulsion type and from hydrogels should be applicable as well to aluminum acetate ointments.

Therefore, four different ointments were prepared: No. 3 below representing an oil/water emulsion and No. 4 a hydrogel. The release of aluminum acetate into agar was compared with the ointments No. 1 and No. 2, both representing water/oil emulsion type ointments. To demonstrate the diffusion, use was made of the color reaction between aluminum hydroxide and sodium alizarine sulfonate as described by Feigl (4).

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### Materials

|                    |  |          |
|--------------------|--|----------|
| Ointment bases.—#1 | Anhydrous Lanolin                                | 5.0 Gm.  |
|                    | Liquid Petrolatum                                | 5.0 Gm.  |
| #2                 | Tevalan anhydr. <sup>1</sup>                     | 5.0 Gm.  |
|                    | Liquid Petrolatum                                | 5.0 Gm.  |
| #3                 | Ungt. Emulsificans Aquosum<br>B. P. <sup>2</sup> | 10.0 Gm. |
|                    |  |          |
| #4                 | Tragacanth Powder (Penick's<br>No. 1, USP)       | 0.4 Gm.  |
|                    | Nipagin "M" (Methylparaben)                      | 0.02 Gm. |
|                    | Distilled water q.s.                             | 10.0 ml. |
|                    |  |          |

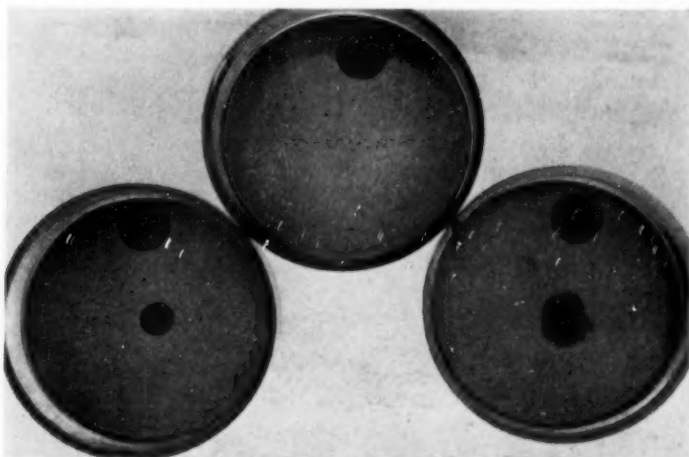
To each of the ointment bases 1 ml. of 8 per cent aluminum acetate solution was admixed until a homogenous product was achieved.

*Agar.*—One hundred milliliters of a 2 per cent agar was heated and 1 ml. of a 0.5 per cent aqueous solution of sodium alizarine

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1. Tevalan, made by TEVA, Middle East Pharmaceutical & Chemical Works, Jerusalem, is described as "absorption base, consisting of paraffins, dekanols and neutral esters of cholesterol."

2. Slightly modified: instead of 1 percent chlorocresol as preservative 0.2 percent Nipagin "M" (methylparaben) was used.





sulfonate added. The stained agar was poured into six Petri dishes, covered with a lid and allowed to cool down to room temperature. (Aseptic technique is required to avoid contamination of the plates.)

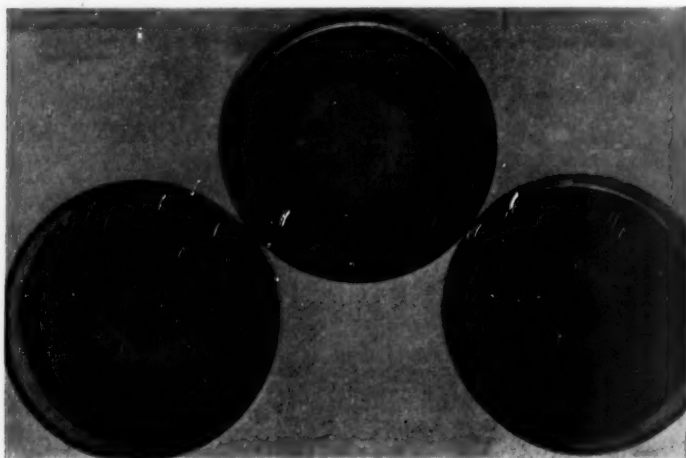
### Experimental

The ointments were applied on the agar surface by aid of a platinum loop. Thus approximately equal quantities of ointments are used. For each ointment one plate was used. The plates were incubated at 37° C. for eighteen hours. After incubation the plates were "developed" by exposing to ammonia (11 N) vapors. The red color changed to violet. In the presence of  $Al^{+++}$  ions a rose to brick-red color appeared, due to formation of an Alizarine-Aluminum lake (4, 5, 6):

Two plates were left without application of any ointment, to serve as "blanks": on plate 5 one drop of 10 per cent acetic acid was placed and on plate 6 one drop of 8 per cent aluminum acetate solution and developed likewise.

### Results

All the five plates, containing 0.005 Gm. per cent sodium alizarine sulfonate, stained deep violet after exposure to the Ammonia vapors. Only the diffusion zones of the  $Al^{+++}$  ions stained rose in contrast with the violet color of the rest of the agar.





There was no diffusion of  $Al^{+++}$  ions into the agar on plates with ointments 1 and 2. This showed that Lanolin and the so-called absorption bases are unsuitable ointment bases for aluminum acetate solution. On the other hand the plates with ointments 3 and 4 exhibited well-defined diffusion zones of  $Al^{+++}$  ions.

### Conclusions

1. Lanolin and other water/oil absorption bases are not suited for ointments containing Burow's solution. As aluminum acetate is not released, the expected astringent effect cannot take place.

2. Ungt. Emulsificans Aquos. B. P., the fat/water ratio of which to be adjusted to give the most suitable consistency, and 4 per cent tragacanth mucilage are equally well serviceable as bases for astringent ointments.

3. The 4 per cent tragacanth mucilage seems to be the base of choice for nasal ointments as its consistency resembles best the normal nasal secretion, it releases freely the incorporated astringent and is non-irritating.

### Summary

A simple spot-analysis method for detection of aluminum ions has been adapted to measure aluminum acetate diffusion from ointment bases. Two ointment bases, widely used in prescriptions of Burow's solution, were found unsuitable for lack of release of the astringent. Two other bases for ointments were tested and proved suitable on account of their good release of the astringent.

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## ANCIENT HERBALS AND ANCIENT THERAPY

By William L. Blockstein \*

**P**HARMACEUTICAL and medical arts and science owe much to early books on herbs and botanicals. These books, or herbals, as they were called, were a happy combination of art, literature, science, and folklore. Their history extends back to the beginnings of recorded events. Among the earliest are the works of Dioscorides and Pseudo-Apuleius and others in the West, and many workers in the East.

Down through the ages, herbs have been used to cure man's ailments, dress his wounds, flavor his food, poison his enemies; and to scent his temples, churches, and palaces. Some of them were dried and burned in hospitals to exhale pleasant fragrances and to overwhelm the stench of sickness. Moreover, they crept beyond the realm of science and went over to an area of magic and superstition and were employed as well in love potions and for both beneficent and malignant charms.

Early apothecaries seemed to play a small part in the development of botanical gardens, herb gardens, and publications relating to both. Among the most prominent was Pierre Phillipe Alyon, apothecary at the Val de Grace Hospital in France. Alyon, who lived between 1758 and 1816, produced a "Tours de Botanique," which was to serve as a text for the education of French children. It is interesting to note that one of those children, both in 1773, became Louis-Phillipe, King of France.

Another apothecary of note is William Curtis (1746-1799) who set himself up as an apothecary in London at the age of twenty. In spite of his business interests, he could not abandon his love of botany. When, at the age of twenty-seven, he was given the post of Praefectus Horti and Demonstrator to the Society of Apothecaries at Chelsea, he jumped at the chance. His duties consisted of familiarizing the

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apprentices of the Apothecaries' Society with the medicinal plants in Chelsea Gardens. Here he began a series of lectures on medical botany, and after he found that the majority of his time would be taken up with this work, he sold out his interest in the apothecary shop and developed the Curtis Garden.

In his garden he cultivated some six thousand species of plants, worked on his first literary efforts, and planned the "Flora Londinensis" to show the plants that grew around London. Another venture of his has existed to this day; this is the world-famed "Curtis's Botanical Magazine," published continuously from 1787.

John Parkinson (1567-1650) was Apothecary to James I and author of "Paradisi in Sole Paradisus Terrestris." After publication of his "Paradisus," he was made Herbalist to Charles I. He was author, too, of "Theatrum Botanicum," published in 1640. His "Paradisus" is considered by Miss Rhode, in "The Story of the Garden," in 1932, as the most important of all seventeenth-century gardening books.

The first German apothecary known as the author of a botanical book of importance was the Nuremberg apothecary, Basilius Bealer (1561-1629) who wrote the "Hortus Eystettensis," a description of the Botanical Garden in Eichstaett, containing more than a thousand illustrations.

Many workers other than apothecaries were concerned with the production of herbals and other botanical works. As mentioned above, Dioscorides, who was a Greek author and physician to the Roman army, produced one of the first medical treatises, which included about five hundred medicinal plants. His work, completed in the first century, A. D., was cited as gospel throughout much of the entire Middle Ages.

Early herbals were produced with laudable motives, as, for example, the "Hortus Sanitatis," or "Gart Der Gesundheit," published by Peter Schoeffer at Mainz, in 1485. In his introduction, Schoeffer states his purpose: "Since man can have no greater nor nobler treasure on earth than bodily health, I came to the conclusion that I could not perform any more honorable, useful or holy work . . . than to compile a book in which should be contained the virtue and nature of many herbs . . . together with their true color and form,

for the help of all the world and the common good." For this worthy endeavor, he employed a "master learned in physic" and a "painter ready of wit, cunning and subtle of hand." Schoeffer's herbal set the pattern for many European herbals that followed his venture and, more than a pattern, served to supply a number of publishers with woodcuts and illustrations that were slavishly copied and re-employed for a period of at least fifty years.

Other herbals of note that are referred to in this study are: The Grete Herball, printed by Peter Treveris in England in 1526; a London volume, Banckes's Herbal of 1525, printed by Richard Banckes; the Leech Book of Bald, an ancient Celtic manuscript; Parkinson's Theatrum Botanicum of 1640; Leonard Fuch's Historia Stirpium of 1542; the Parisian volume, Le Grand Herbiere of about 1504; the Chinese herbal, Rh-vu, which dates from about the fifth century, B. C.; the Goodman of Paris, which was written in 1393; the Vertuose Booke of Distylacyon; and Rembert Dodoen's work, A Nieuwe Herball, London 1578.

In examining the books that included quotations from these early herbals, it appeared that a review of early attempts at medical therapy might prove of interest. It must be borne in mind that the following list makes no attempt at completeness, and that the purpose of this study was to interest others to cover the same sources in order to stimulate a review of early curative plant parts.

"Banckes's Herbal" discusses many plants in its pages. Anise, for example, is considered in this manner: "The virtue of this herb is thus, it unbindeth the stopping of the liver and of wicked winds and of great humors." Sage, states Banckes, is used in the treatment of poisoning. "Seeth sage in ale or wine and use it to drink in three days, and thou shall be whole, by the grace of God." According to the same source, "Agrimony is especially good to heal a wound that is with iron." Galen is quoted by Banckes as having used the drawn juice of celandine, "meddeled with white wine and annoint the visage therewith, and it shall do away with freckles of the visage." Celandine was also good for cankers in a man's mouth, and for "sore eyes." Ground ivy had many users in early times. The "Leech Book of Bald," III 29, says, "For sunburn, boil in butter tender ivy twigs; smear therewith." Banckes goes further than just sunburn, and recommends that this herb "sodden with swine's grease

is a good ointment for all manner aches." Greek mythology enters our discussion, for Banckes points out that yarrow was "found by King Achilles, and with it he healed his men that were wounded with iron. For wounds, stamp this herb with swine's grease and plaster it to the wound, and it shall heal it." It also enjoyed some popularity for severe cases of vomiting, as "for him that may not hold his meat, let him stamp yarrow with wine, and drink it warm." In the same form, it was used for stopping "heartburning." Banckes recommends sweet bay in this monograph—"Bay is good to purge a man of phlegm and of the choler. It is good for a man that may not hear, for if the juice thereof be put in his ears . . . it will heal it." Many writers referred to the invigorating effects of borage. Banckes goes further and flatly says, "Borage water drunk with wine maketh a man glad and merry." Could this effect be gained by wine alone? Dill was used thusly by Banckes, "It assuageth rumbling in a man's stomach. Also it destroyeth hiccups. The seed of this herb burnt and laid upon a wound, it healeth soon." Elecampane was to be eaten by a man with sagging teeth to fasten them again, according to our Mr. Banckes. Nothing seemed to be overlooked by this gentleman, as we can see by his remedy for loss of hair. "Caraway is good for restoring hair where it hath fallen away." He adds that it is good, as well, for "the frenzy and for biting of venomous beasts," and that "it destroys wicked winds and the cough." Mints, such as peppermint, were used by Banckes to "give a sweet-smelling mouth" if rubbed on the teeth; used as a poultice, it would cure "botches on the face."

Dioscorides, who was quoted again and again, had many interesting comments on herbs of his day. He recommended caraway for its "warming" effect, saying that "it is good for the stomach." Dioscorides recognized thyme early for its beneficent action in coughs, which preceded its present-day use in a cough preparation by some eighteen centuries. At that time he said, "mixed with honey, prescribe it for driving out phlegmy matter from the thorax, for asthma"; this not being enough for the herb, he adds another use, "for expelling worms." Much earlier than Banckes's is his description of the use of agrimony, "Being beaten small when it is green, it hath the power to cure cuts." "The well scenting" roots of iris, said Dioscorides, are good for the "bites of venomous beasts" and "sun burning."

The Grete Herball has a different use for iris. It states, "To make good colour in the face, take the knottes that growe about the rote of wylde lyllyes and drye them and make powdre of them and tempre the powdre in rose water and then dryed and derue it so thre or iiii times. And than with the same powdre in rose water anoynte ye face." Black hellebore, according to the Grete Herball, will cure gout, "scruff of the head," and "scabies." Sweet bay was recommended in the Grete Herball for colic; "a bath made of bay leaves is good"; also "against the evil color of the face . . . and against all manner of red things that come in young folks faces . . . take new bay berries and put out the hulk and make fine powder and put it in honey and annoint or bathe the face."

Pseudo-Apuleius, a sixth-century writer, who regarded physicians with complete distrust, had his own ideas on plant treatments. Among other comments, he stated, "For the disease which is called lethargy, and in our language is denominated forgetfulness, take the wort Rue, washed in vinegar, souse then the head therewith." As a use for columbine, he claims that "if any one have with him this herb . . . he will not be barked at by dogs." He considered pennyroyal to be a valuable remedy for seasickness. He says, "If any endure nausea on shipboard, let him take the herb pennyroyal and wormwood, let him pound them together with oil and with vinegar and let him smear himself therewith frequently."

The "Hortus Sanitatis" ascribed many strange and mysterious powers to periwinkle. It was to be carried with a man next to his skin, so that "the devil hath no power over him who bears it." "No witchery may enter the house which has this herb hanging over the door and if any witchery be already in it will be driven out soon." It had more practical application for "staying the flux," easing the toothache," and to "drive out the wicked fever that come of severe cold." Bugloss, according to the "Hortus Sanitatis," "is good for him who has harmful wicked moistness of the lung" and "a bad cough." Schoeffer has a prescription for heart disorders in the "Hortus" that reads thusly, "A half-pound of these sweet smelling flowers (of lily of the valley) soaked in a liter of wine for four weeks, then distilled, then mixed with the resulting liquor with four peppercorns and a little lavender water." If troubled with apoplexy, "Drink thereof, and fear not of a stroke that month."

Belladonna is mentioned in "Le Grand Herbar" of 1504. In 1542 Leonard Fuchs included it in his "Historia Stirpium" and recognized its poisonous properties. Its earliest use appears to be that employed by Venetian women who made a distilled water of the plant for cosmetic purposes. They felt that because of its property of enlarging the pupils of the eyes, it added to their beauty and appeal.

The Dodoens book, "A Nieuwe Herball," quotes Dioscorides as saying, "It is good against the byting of Madde Dogs, to bruse the leaues of Pantayne and lay therevpon, or to poure of the iuyce of Plantayne into the woundes. . . ."

Parkinson's "Theatrum Botanicum" recommends, "The distilled water of thyme applied with vinegar of Roses to the forehead is a great helpe to cure one of the Frensy.".

"The Goodman of Paris," written by an old gentleman who took a young bride, is a homey tome. It is a combination cook book, helpful hints for the newly wed, and a medical text. One of the passages in this book describes how to cure a toothache by breathing "the steam of boiling water into which sage and other herbs" have been "set."

"The Vertuose Boke of Distylacyon" states that the leaves and flowers of the cowslip distilled in water "is good against the pain in the head coming from cold."

There are many other passages that could be cited from books on herbals, or from the herbals themselves. There is much to be said for the authors of these and similar works, who tried in their way to advance the fight against illness. They advocated many odd ideas of therapy, laid the basis for the science of botany, and provided food for thought for students of later years. As a poignant example, there is a quote from "Gerard's Herball" on foxglove. He says, "The fox-gloves in that they are bitter, are hot and dry, with a certaine kind of clensing qualitie joyned therewith; yet they are of no use, neither have they any place amongst medicines, according to the Antients."

Not long after, an English physician became famous for his infusion of fox-glove, which is the basis for all of today's digitalis therapy.



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## ANGINA PECTORIS

### A Review

**A**NGINA PECTORIS is itself a symptom and not a disease. This term—often shortened to simply, angina—is used to describe attacks of paroxysmal pain in the chest; this pain is a symptom of some serious cardiac disturbance. Angina is also known as angina of effort, breast pang, sternalgia, sternodynia, and orthopnoea cardica.

The immediate cause of angina is believed to be a relative anoxia of the heart muscle which occurs whenever the demands upon the heart exceed those which can be met by the available blood flow. This takes place, usually, when the coronary circulation is inadequate so that insufficient oxygen is carried to the heart muscle. In severe cases, the anginal attacks may occur even when the patient is at rest and, then, the prognosis is not good. In less severe cases, the attacks occur only during physical or mental stress.

While the immediate cause of angina is anoxia of the heart muscle, other conditions are responsible for this failure of sufficient blood and oxygen to reach this area. The most common cause of coronary insufficiency is coronary sclerosis, although other conditions may also produce anoxia of the heart muscle. In coronary sclerosis, there are arterio-sclerotic changes causing a thickening of the blood vessels supplying the heart muscles. In some cases, this proceeds until there is a complete occlusion. Such barriers to blood flow are responsible for the development of anoxia in those areas of the heart muscle supplied by such vessels.

Severe anemia has been known to cause angina since the oxygen carrying power of the blood is greatly reduced.

There are many precipitating factors which may act as a "trigger-mechanism" and induce angina. These are excitement, mental strain, physical effort, a heavy meal, infections, exposure to cold, etc.

### Symptoms

An anginal attack usually follows a typical pattern. First, there appears the sensation of heaviness in the chest, followed by the onset of actual pain. The pain may be either substernal or to the left of

the sternum, and it varies greatly in intensity. The pain often radiates to the left shoulder and arm end, sometimes, into other areas such as the jaw, back, etc. Usually, the pain does not last more than a few minutes, but it is accompanied by a feeling of suffocation. A typical characteristic of anginal pain is the relief provided by nitrites. If the pain lasts for more than thirty minutes, it is highly suggestive of an occlusion.

The clinical course of angina is quite variable. Some patients have a mild attack not followed by another for a long time. Others may have severe and frequent attacks.

### Diagnosis

The characteristic substernal pain produced by effort is a cardinal sign of angina as is its relief by nitrites. When there is doubt, an exercise test is often used by the physician. This consists of walking over a two-step staircase at a standard rate of speed until pain or dyspnea (shortness of breath) occurs. Such exercise produces characteristic changes in the electrocardiograms of most patients who have angina. The exercise test is also believed by some to provide a means of determining the patient's response to drug therapy. Care in the use of this test on patients is necessary and it should not be used in cases with severe angina or an infarction.

Other diagnostic tests, such as the anoxemia test, are sometimes used. In this, a mixture, poor in oxygen (90% nitrogen-10% oxygen), is inhaled by the patient and electrocardiograms taken.

### Prognosis

The outlook for any given patient is uncertain and it depends on many factors. If the attacks are mild and brought on only by unusual circumstances, the patient may live for many years. On the other hand, death may result from a single attack. The average life span following the first attack is probably eight to ten years assuming care and proper medication.

### General Measures

There are many general measures which should be taken by the angina patient to reduce the incidence and severity of attacks. He should stop all activity at the first indication of substernal discomfort since this tends to reduce the demands made upon the heart. Over-

weight is objectionable and an effort should be made to correct this in the obese. Anemia, if present, should be treated. Smoking is not desirable since it both increases the heart rate and reduces, somewhat, the oxygen carrying capacity of the blood. Exposure to cold is also undesirable since this causes reflex constriction of the coronary arteries.

### Drugs Used in Angina

There are two (and, possibly, three) therapeutic approaches in the treatment of angina. One type of drug is used specifically to relieve the attack. A second group is used for the purpose of reducing the incidence of the seizures. A third group of drugs is presumed to arrest or retard the arteriosclerotic changes in the coronary vessels.

*Nitrites* are the most valuable group of drugs to relieve angina attacks. Their ability to relax the arteries of the coronary tree is the fundamental basis of their use.

*Amyl nitrite* (iso-amyl) and *octyl nitrite*, by inhalation, are very rapid in their effects and are often prescribed by the physician so that the patient may use them at the first sign of an approaching attack. Amyl nitrite is usually supplied in small "pearls" which can be crushed in the handkerchief or some other absorbent material and the vapor inhaled. Relief, usually, is provided within one minute. The usual dose is 0.2-0.3 cc. Octyl nitrite is available in an inhaler with the drug present absorbed in some porous material. It acts similarly to amyl nitrite but it is claimed to be more stable, less toxic, less disagreeable in odor, and to produce less methemoglobinemia with protracted use.

*Organic nitrates* are therapeutically useful and they are believed to act by forming nitrite ions in the body.

*Nitroglycerin* (glyceryl trinitrate) is widely used in angina pectoris and is preferred by many over the alkyl nitrites for the relief of attacks. It is best administered in the form of soluble tablets held under the tongue. The dose used is the smallest which will provide relief so as to avoid side-reactions. The required dose varies from 0.15-0.6 mg. The effect of the drug so administered is usually observed in two to three minutes. Side-reactions sometimes observed are headache, dizziness, and flushing of the face.

Nitroglycerin is rather transient in its effect and patients are usually advised to use it as frequently as necessary to prevent attacks. Its use as a prophylactic to abort an attack when one is impending is quite common.

Other organic nitrates are available which are less transient in their action than is nitroglycerin. These include *erythrityl tetranitrate*, *mannitol hexanitrate*, and the more recently released, *pentaerythritol tetranitrate*. Erythrityl tetranitrate and mannitol hexanitrate are given in doses of 15-60 mg. and their effects begin in fifteen to thirty minutes and last for three to four hours. The drug, pentaerythritol tetranitrate (Peritrate—Chilcott Laboratories), is claimed to be particularly useful in angina, reducing both the frequency and the severity of attacks. It is also claimed to cause fewer side-effects. Like the other organic nitrates having a prolonged action, it is used primarily to prevent attacks since it is too slow to relieve an acute attack. In acute attacks, the more rapid drugs; e. g., amyl nitrite and nitroglycerin, are preferred. The usual dose of pentaerythritol tetranitrate is 10 mg. given three to four times daily. All of the organic nitrates are highly explosive in pure form and, consequently, they are distributed only well-diluted with an inert substance; such as, sugar or lactose.

*Sodium nitrite* is still used by some physicians for the prevention of anginal attacks. It is not considered as desirable as the organic nitrates since it often causes gastric irritation. The usual dose of sodium nitrite is 60 mg. given two to three times a day.

*Papaverine* has been reported as useful in angina but not all investigators are agreed as to its value. In experimental animals, it does increase coronary blood flow but the effect is transient. The oral dose of papaverine hydrochloride is 100-200 mg., three to four times a day. A closely related drug, *Paveril Phosphate* (Lilly), differs from papaverine only in the presence of a methyl group at position 3 of the isoquinoline ring and an ethoxy group at position 4 on the benzene ring instead of a methoxy. Paveril Phosphate is claimed to produce much less side-reaction than papaverine; it is given in a dose of 0.2 gm., three to four times a day.

A number of the *xanthine derivatives*; chiefly, *theophylline* and *theobromine* and their preparations, are used in the prophylaxis and

treatment of angina, although there is considerable debate as to their exact value. Aminophylline (theophylline ethylenediamine) seems to be the most popular drug in this group. It is administered orally, in suppositories, and by injection. The oral dose is 0.1-0.2 Gm., three times daily. The intramuscular dose is 0.2-0.5 Gm. Other xanthine drugs used in angina are theobromine sodium salicylate (Diuretin), theobromine sodium acetate, and theobromine calcium salicylate (Theocalcin), theophylline (Theocin), and theophylline sodium acetate (Theocin Soluble).

*Barbiturates*; principally, *phenobarbital*, are frequently combined with the xanthines as they are with other drugs in the treatment of angina. The purpose is to keep the patient calm since it is well known that emotional stress often precipitates an attack. Often, when there are closely recurrent attacks of angina, it becomes necessary to break them up by giving barbiturates to the point of semi-narcosis for a day or two.

*Testosterone propionate* and *methyltestosterone* have been advocated by some in the treatment of males with angina but their value is highly controversial. It would seem that some men are benefited by androgen therapy when their angina is associated with the male climacteric. Testosterone does seem to possess some vasodilator action and to increase the sense of well-being. It must, however, not be given to the point that the patient's well-being and drive cause him to exceed his cardiac reserve.

*Alcohol*, in moderate quantities, is often prescribed by the physician for the patient with angina. It is believed to have value because of its well known vasodilator action. Here again, however, it is potentially hazardous should it, by depressing the inhibitions, cause a patient to engage in activities requiring physical exertion.

*Cobra venom* has been used in angina; it seems to increase the exercise tolerance of the patient but does not alter the changes in the electrocardiogram produced by exercise. It is quite possible that its effect is largely that of an analgesic since cobra venom is also used to relieve intractable pain as a substitute for morphine. The dose is 10 mouse units given intramuscularly.

*Nicotinic Acid* given orally does not seem to be of value in angina since the dose required to produce beneficial results causes excessive peripheral flushing. When given intravenously, however, in doses of 100-300 mg. twice weekly, some value has been reported.

*Khellin* is a principle obtained from the plant *Ammi visnaga*. It is known under a variety of names including visammin and amio-cardine. Proprietary products of it are available under the titles Ammivin and Eskel.

*Khellin* is claimed to increase the coronary circulation much more than does aminophyllin and to have a greater duration of action. It is used chiefly to prevent attacks. Some side-reactions; including nausea, anorexia, and dizziness, may be observed and may require a reduction in dose. The preparations available determine the precise dosage. Highly purified products are usually given initially in a dosage of 20-40 mg. per day with the dose gradually increased by 20-40 mg. at weekly intervals until an adequate response is shown without serious side-effects.

*Thiouracils*; such as *methyl thiouracil*, *propyl thiouracil*, and other antithyroid drugs, may have value by decreasing the patient's basal metabolic rate and, thus, reducing the work required of the heart.

### Lipotropic Factors

The rationale for the use of such drugs as methionine and choline is highly debatable. Some authorities claim that these substances arrest and, possibly, reverse the atherosclerosis responsible for the narrowing of the coronary arteries. Others claim that their effect is purely that of coronary vasodilation. Choline as the chloride or dihydrogen citrate is the drug in this group most commonly employed. The dose given varies from 1.5-6.0 Gm. per day, based upon the tolerance of the patient.

### Surgery

Certain surgical procedures are sometimes resorted to in angina when other measures fail. These procedures are of two types. In one type, the nerve fibers which carry painful stimuli to the central nervous system from the heart are blocked with drugs or severed. The second type is concerned with improving the blood supply to the heart muscle.

In the first instance, paravertebral block may be employed. Here, alcohol is injected into the sides of the upper four or five thoracic vertebrae to paralyze the sympathetic ganglia. Sometimes, actual severance of various dorsal and cervical sympathetic fibers is carried out.

Operations to produce collateral circulation in the heart are varied in nature but all are based upon the attachment of some vascular tissue to the heart. Grafting tissue on the myocardium can produce collateral circulation either by the formation of new collaterals within the heart and stimulating the size and function of those already present or by the formation of new channels from the grafted tissues.

The development of an adhesive pericarditis by the dusting of talc on the exposed pericardium is claimed to be of value. The hyperemia which accompanies the inflammation is claimed to open up the anastomosing channels between the coronary arteries and also to form new channels. The end result is an improved blood supply to the heart muscle.



**Role of the Lungs in Regulation of the White Blood Cell Level.** Ambrus, Clara M., Ambrus, Julian L., Johnson, Gilbert C., Packman, Elias W., Chernick, Warren S., Back, Nathan, and Harrison, Joseph W. E. *Am. J. Physiol.* 178:33 (1954). In Starling heart-lung preparations of dogs, circulating white blood cells are rapidly removed until a certain level is reached. This level is maintained for the entire useful life of the preparation. The level is independent of the leukocyte count of the infused blood. It was not possible to exhaust this white cell removing ability of the lungs by frequently introducing new samples during several hours. Such results are obtained whether the circulating blood originates from the same individual or from homologous or heterologous donor species, whether the blood is heparinized or defibrinated.

The removal affects mainly the granulocytes and, only secondarily, other white cells. The red blood cell level does not change in these experiments.

Introduction of white cell poor blood into heart-lung preparations results in release of white cells from the lungs. Using  $P^{32}$  labeled cells, this phenomenon was found to be at least partly due to mixing with residual blood.

Similar phenomena to the above were observed in heart-lung preparations cross-transfused with the circulation of intact donor dogs without the use of anticoagulants.

Thorotrast, a powerful inhibitor of the phagocytic activity of the reticulo-endothelial system, does not affect the leukocyte removing ability of the lungs.

*In vivo* cardiac and pulmonary catheterization experiments in dogs revealed a difference between leukocyte counts of blood entering and leaving the lungs. The prolonged presence of catheters induces fluctuations in the leukocyte level. In short range experiments, however, no such fluctuations occurred. Statistically significant difference was found in total leukocyte count in blood samples before and after passing through the lungs. Similar differences were found in polymorphonuclear neutrophil counts but not in the case of other blood cell types. Analysis of covariance revealed correlation between the decrease of total leukocyte count and that of the neutrophil count during passage through the lungs. Similar results were obtained from various locations by direct punctures.

It is concluded that the lungs play an important role in the physiologic disposition of leukocytes and in the regulation of the white blood cell level of the blood.



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